ABSTRACT

Bifunctional molecules comprising two hsp-binding moieties which bind to hsp90 in the pocket to which ansamycin antibiotics bind connected via a linker are effective for inducing the degradation and/or inhibition of HER-family tyrosine kinases. For example, a compound of two geldanamycin moities joined by a four-carbon linker provides selective degradation of HER-family tyrosine kinases, without substantially affecting other kinases. These compounds can be used for treatment of HER-positive cancers with reduced toxicity, since these compounds potently kill cancer cells but affect fewer proteins than geldanamycin.